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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,767	02/10/2004	Lester Earl Casida JR.	8014-020-999	3630

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/776,767	CASIDA ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-89* is/are pending in the application.

4a) Of the above claim(s) *78,79 and 81-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-77, 80 and 86-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 68-77, 80 as amended and new claims 86-89 (6/15/2007) are under examination in the instant office action.

Applicant's election with traverse of the Group I and the species of "living whole cells" in the reply filed on 11/03/2006 was acknowledged in the last office action. Thus, this application contains claims 78,79 and 81-85 drawn to an invention nonelected with traverse in reply filed 11/03/2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

Written description

Claims 68-77, 80 as amended and new claims 86-89 remain/are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as explained in the last office action.

Claims are directed to a method for treating or inhibiting a disease of an animal, said disease caused by a microorganism wherein the method comprises administering to said animal an effective dose of an antimicrobial preparation comprising living cells of *Burkholderia casidae* or variant thereof.

The limitation "an effective dose "of *Burkholderia casidae* or variant thereof in the method for *in vivo* treating or inhibiting diseases of animals or humans lacks support in the instant specification. This limitation is neither has literal support in the as-filed specification by way of a generic disclosure, nor are there specific examples of using the applicants' *Burkholderia casidae* or variant thereof in the method for *in vivo* treating or inhibiting a disease of an animal or a human that would show possession of the concept of using any and all "effective dose(s)" for any and all infections listed in claims 70-73, 86, 87. There is only a generic phrase that *Burkholderia casidae* may be used in the prevention and/or treatment of microbial diseases of plants and animals (page 4, last line) including humans (page 5, line 3). These phrases are a mere suggestion not a written description of *in vivo* treating or inhibiting diseases of animals or humans. The specification does not even describe those bacteria, yeasts, fungi or alga that are considered as causing diseases of animals. The specification describes plant pathogens and treating plant diseases but not the animals and humans. In fact, most of the described infections are established plant pathogens, for example: *Alternaria, Botrytis*, etc. Thus, one skilled in the art cannot visualize or recognize what would be protocol of treatment and/or the effective doses of *Burkholderia casidae* including effective doses of living cells of *Burkholderia casidae* treating infections in animals or humans.

Given the total lack of any description of "effective" doses for *Burkholderia casidae* or variant thereof in the method for in vivo treating or inhibiting a disease of an animal or a human, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Enablement

Claims 68-77, 80 as amended and new claims 86-89 remain/are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention as explained in the last office action.

Claims are directed to a method for treating or inhibiting a disease of an animal, said disease caused by a microorganism wherein the method comprises administering to said animal an effective amount of an antimicrobial preparation comprising living cells of *Burkholderia casidae* or variant thereof.

The claimed *Burkholderia casidae* or variant thereof has a 16S rRNA gene comprising a sequence that is at least 97% similar to the sequence of SEQ ID NO: 1 and characterized by a particular cellular fatty acid composition. Some claims are further drawn to the used of a particular strain 2.2N (ATCC 55961).

Some claims are further drawn to the antimicrobial activity against bacteria including *Nocardia, Staphylococcus aureus or Streptomyces*, to the antimicrobial activity against yeasts including *Saccharomyces cerevisiae, Candida albicans or Cryptococcus neoformans*; to the antimicrobial activity against fungi including *Aspergillus niger, Penicillium*; to the antimicrobial activity against alga such as is *Anabena.*

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of

one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The nature of the invention is discovery of a novel strain of *Burkholderia casidae* that is useful as biocontrol agent of plant pathogens.

The breadth of the claims are drawn to the use of *Burkholderia casidae* as a probiotic or to the use of whole living cells of *Burkholderia casidae* or variant thereof including strain ATCC 55961 for *in vivo* administration to animals including humans. The claimed bacteria is a novel strain as established in the parent application (now US 6,319,497) and it is used for treating plant diseases (US 6,689,357).

However, the instant specification does not support the scope of the claims drawn to the use of living cells of *Burkholderia casidae* or variant thereof including strain ATCC 55961 for *in vivo* administration to animals including humans as intended for treating and inhibiting microbial infection. The "effective" dose for *in vivo* administration and *in vivo* treating or inhibiting microbial infections in animals or humans are not disclosed in the specification by way of generic disclosure or in the working examples. The applicants' working examples are only limited to the *in vitro* testing of *in vitro* antimicrobial activities of the claimed bacteria on agar plates and to treating plants infected with plant pathogens. There is no a single example with any animal model.

The state of the prior art demonstrates that some bacteria belonging to the claimed genus of *Burkholderia* including species of *B.cepacia* that is closely related to the applicants' strain (se

specification table 3, page 25) have been reported as opportunistic human pathogens, they were isolated from clinical specimens of diseased patients and some of them were associated with cystic fibrosis, for example: see introduction of the reference by Tabacchioni et al. (IDS reference; Res. Microbiol. 1995, 146, 531-542). The applicants' novel strain has been isolated from soil (specification page 16, lines 20). However, the reference by Tabacchioni et al. teaches that some human pathogens can be isolated from soil or from the same ecological niche as the plant-growth promoting bacteria (page 532, col.1, lines 6-9) and that screening for potential pathogenicity of soil isolates would be needed. The instant applicants does not describe any testing that would involve animal or human models. Thus, the claimed concept of using the applicants' novel strain of *Burkholderia casidae* for *in vivo* administration for treating animal diseases is uncertain and unpredictable in the absence of at least some potential pathogenicity testing.

Further, in alternative, even if the applicants' novel strain of *Burkholderia casidae* might not be an animal or human potential pathogen, the fact that it was isolated from soil clearly demonstrates that this strain is not a normal inhabitant of animals or humans. The state of prior art teaches the characteristics of a good probiotic fro treating animal or human infections such as being a normal inhabitant of the site of application, capable of surviving and growing in the site of application, capable to exert beneficial effects on the host, etc., for example: see page 312 of the reference by O'Sullivan et al. (Trends in Food and Technology. 1992, vol. 3, page 309-314). The instant application is silent about ability of the claimed *Burkholderia casidae* to adhere, to survive, to colonize and to grow on animal or humans tissues *in vitro* and/or at the site of *in vivo* applications. No animal or human model is shown by applicant to support enablement of the

claimed concept of treating or inhibiting undesirable microorganisms in the animals or humans including inhibiting the bacteria, yeast, fungi and alga that are listed in the instant claims 70-73, 86 and 87.

Therefore, neither specification nor the prior art can be said to support the enablement of the claims over their breath.

Undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary because of the limited amount of guidance and absence of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art. Without sufficient guidance administration of the applicants' strain as currently claimed is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. As set forth in *In re Fisher*, 427 F2.d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.
In cases involving unpredictable factors, such as in vivo physiological activity of therapeutic agent, the scope of the enablement varies inversely with the degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

Thus, the scope of the claims is not commensurate with the teachings of enablement of the specification.

Response to Arguments

Applicant's arguments filed 6/15/2007 and Declaration by J. O. Falkinham filed on 6/15/2007 have been fully considered but they are not persuasive.

With regard to the claim rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement Applicants argue that neither literal description nor working examples are required to satisfy the written description requirement (response pages 6-7), thereby, admitting that both literal description and working examples of a method for *in vivo* treating or inhibiting a disease of an animal by administering to said animal *Burkholderia casidae* is truly lacking in the as-field specification.

Applicants argue that a person skilled in the art at the time the application was first filed based on the teaching of the specification coupled with knowledge common in the art at that time, would readily appreciate that the inventors were in possession of an "effective dose" of *Burkholderia casidae* for *in vivo* treating or inhibiting a disease of an animal because standard tests such as the disc diffusion tests that are described in the instant specification could be used to routinely calculate an effective dose of an antimicrobial preparation comprising a substantially pure culture of *Burkholderia casidae*. This argument is not found particularly convincing. First, the elected invention is directed to the "living whole cells" as therapeutic agent and the disc diffusion tests or agar diffusion tests are based on activity of the antimicrobials secreted by the microorganism into the cultivation medium. Thus, applicants main argument is directed to the products separated from cells of *Burkholderia casidae* rather than to the "living whole cells". Nevertheless, considering the fact the working examples disclosed in the as-filed specification when taken as a whole describe the use of *Burkholderia casidae* culture, filtrate or cell-free fractions as a biocontrol agent for the diseased plants, one of ordinary skill practitioner would appreciate that the inventors were in possession of using a plant biocontrol agent but not a

therapeutic agent. Appreciation of using *Burkholderia casidae* as a therapeutic agent would be a realization of some novel use that is neither described nor conceived in the as-field specification.

Although disc diffusion tests are used to estimate MIC (minimal inhibitory concentration), the culture of *Burkholderia casidae* and/or its effective dose is described in the instant specification as biocontrol agent of diseased plants. Although some pathogens could cause diseases in plants and in animals, the culture of *Burkholderia casidae* and/or its effective dose is described in the instant specification as a plant biocontrol agent not a therapeutic agent.

Thus, the claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to the claim rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement Applicants argue that amount of guidance disclosed in the working examples drawn to *in vitro* testing is sufficient for one skilled in the art to utilize these results to routinely calculate effective dose for *in vivo* administration and that office action is missing reason for conclusion about the lack of correlation between *in vitro* model to the claimed method.

The elected invention is directed to administration of "living whole cells". It was noted in the last office action that with regard to selection of microbial cells for administration of to animals and humans the state of prior art teaches the characteristics of a good probiotic as therapeutic agent for treating animal or human infections are such as being a normal inhabitant of the site of application, capable of surviving and growing in the site of application, capable to

exert beneficial effects on the host, etc., for example: see page 312 of the reference by O'Sullivan et al. (Trends in Food and Technology. 1992, vol. 3, page 309-314). The instant application is silent about ability of the claimed *Burkholderia casidae* to adhere, to survive, to colonize and to grow on animal or humans tissues *in vitro* and/or at the site of *in vivo* applications. No *in vitro* animal or human model is shown by applicant to support enablement of the claimed concept of using cells of *Burkholderia casidae* for *in vivo* treating or inhibiting undesirable microorganisms in the animals or humans.

Further, it was noticed in the last office action the state of the prior art demonstrates that some bacteria belonging to *Burkholderia* including species of *B.cepacia* that is closely related to the applicants' strain (se specification table 3, page 25) have been reported as opportunistic human pathogens. The specification is silent about virulence of the cells of *Burkholderia casidae* towards animal and humans. Thus, the correlation between the MIC (minimal inhibitory concentration) towards microbial pathogens for the claimed whole culture, culture filtrate and/or unidentified cell-free fractions of *Burkholderia casidae* obtained in the *in vitro* disc diffusion tests as argued is unpredictable for calculation of therapeutic doses in animal and humans because these doses are potentially virulent or at the very least have unpredictable effects.

Thus, the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber, can be reached at (571) 272-0925.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova
AU 1657
September 1, 2007

VERA AFREMOVA
PRIMARY EXAMINER